

WHAT IS CLAIMED IS:

1. A recombinant *C. elegans* that expresses a detectable marker in a dopamine neuron.

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2. The recombinant *C. elegans* of claim 1, wherein the detectable marker is further defined as a marker that can be visually detected.

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3. The recombinant *C. elegans* of claim 1, wherein the detectable marker is further defined as a marker that can be spectroscopically detected.

4. The recombinant *C. elegans* of claim 1, wherein the detectable marker is a green fluorescent protein.

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5. The recombinant *C. elegans* of claim 1, wherein the detectable marker is a yellow fluorescent protein.

6. The recombinant *C. elegans* of claim 1, wherein the detectable marker is a blue fluorescent protein.

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7. The recombinant *C. elegans* of claim 1, wherein the detectable marker is a red fluorescent protein.

8. The recombinant *C. elegans* of claim 1, wherein the detectable marker is β -galactosidase.

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9. The recombinant *C. elegans* of claim 1, wherein the detectable marker is under the control of a promoter.

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10. The recombinant *C. elegans* of claim 9, wherein the detectable marker is an antigenic polypeptide.

11. The recombinant *C. elegans* of claim 9, wherein said promoter is a tissue-specific promoter.

5 12. The recombinant *C. elegans* of claim 11, wherein the tissue-specific promoter is a neuronal promoter.

13. The recombinant *C. elegans* of claim 12, wherein the neuronal promoter is a dopamine transporter promoter.

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14. The recombinant *C. elegans* of claim 13, wherein the neuronal promoter is a tyrosine hydroxylase promoter.

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15. A method of screening for substances that affect neuronal viability comprising:
a) providing a recombinant *C. elegans* that expresses a detectable marker in a neuronal cell;
b) exposing said *C. elegans* to a candidate substance; and
c) detecting a change in the expression of the marker relative to the expression of the marker before said exposing;

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wherein a change in the expression of the marker corresponds to a change in the viability of the neuron.

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16. The method of claim 15, further comprising detecting the expression of the marker in the neuronal cell in the absence of said candidate substance.

17. The method of claim 15, wherein said substance is a neurotoxic substance.

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18. The method of claim 17, wherein the neurotoxic substance is 6-hydroxydopamine, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, or 5,7,di-hydroxy tryptamine.

19. The method of claim 17, wherein the neurotoxic substance is 6-hydroxydopamine.

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20. The method of claim 17, wherein the neurotoxic substance is a generator of free radical species.
- 5 21. The method of claim 15, wherein said substance is a neuroprotective substance.
22. The method of claim 21, wherein the neuroprotective substance is a dopamine transporter antagonist.
- 10 23. The method of claim 22, wherein the dopamine transporter antagonist is imipramine.
24. The method of claim 22, wherein the dopamine transporter antagonist is an amphetamine.
- 15 25. The method of claim 22, wherein the dopamine transporter antagonist is cocaine.
26. The method of claim 21, wherein the neuroprotective substance is a free radical scavenger.
- 20 27. The method of claim 15, further comprising the step of exposing said *C. elegans* to a known neurotoxin prior to step b).
28. The method of claim 15, further comprising the step of exposing said *C. elegans* to a known neurotoxin after step b).
- 25 29. The method of claim 15, wherein the substance is encoded by a polynucleotide.
30. The method of claim 15, wherein the polynucleotide encodes a dopamine transporter regulatory gene, or a gene that suppresses free radical generation.
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31. The method of claim 15, wherein the substance is a polypeptide.
32. The method of claim 31, wherein the polypeptide encodes a dopamine transporter regulatory polypeptide, or a polypeptide that suppresses free radical generation.
- 5 33. The method of claim 15, wherein the substance is a naturally occurring product.
34. The method of claim 15, wherein the substance is a man-made chemical.
- 10 35. The method of claim 34, wherein the man-made chemical is a monoamine oxidase inhibitor.
36. The method of claim 35, wherein the monoamine oxidase inhibitor is a hydrazine derivative.
- 15 37. The method of claim 36, wherein the hydrazine derivative is phenelzine or isocarboxazid.
38. The method of claim 35, wherein the monoamine oxidase inhibitor is a non-hydrazine derivative.
- 20 39. The method of claim 38, wherein the non-hydrazine derivative is tranylcypromine, or pargyline.
- 25 40. The method of claim 15, wherein the substance is an environmental toxin.
41. The method of claim 40, wherein the environmental toxin is a pesticide, or a herbicide.
- 30 42. The method of claim 41, wherein the pesticide is rotenone.

43. The method of claim 15, further comprising:
- a) exposing said *C. elegans* to a known neurotoxin; and
 - b) detecting a change in expression of said marker.

5 44. The method of claim 15, wherein the change in marker expression can be an increase in the marker.

45. The method of claim 15, wherein the change in marker expression can be a decrease in the marker.

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46. The method of claim 15, wherein the detectable marker is further defined as a marker that can be visually detected.

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47. The method of claim 15, wherein the detectable marker is further defined as a marker that can be spectroscopically detected.

48. The method of claim 47, wherein the detectable marker is a green fluorescent protein.

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49. The method of claim 47, wherein the detectable marker is a yellow fluorescent protein.

50. The method of claim 47, wherein the detectable marker is a blue fluorescent protein.

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51. The method of claim 47, wherein the detectable marker is a red fluorescent protein.

52. The method of claim 15, wherein the detectable marker is β -galactosidase.

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53. The method of claim 15, wherein the detectable marker is under the control of a promoter.

54. The method of claim 15, wherein the detectable marker is an antigenic polypeptide.

55. The method of claim 15, wherein the detectable marker is under the control of a neuronal-specific promoter.

56. The method of claim 55, wherein the neuronal-specific promoter is a dopamine transporter promoter.

57. The method of claim 55, wherein the neuronal-specific promoter is a tyrosine hydroxylase promoter, a *cha-1* promoter, an *acr-2* promoter, an *unc-30* promoter, an *unc-4* promoter, or an *asi* promoter.

58. The method of claim 15, wherein the neuronal cell comprises a dopaminergic neuron.

59. The method of claim 15, wherein the neuronal cell comprises a cholinergic neuron.

60. The method of claim 15, wherein the neuronal cell comprises a GABA-ergic neuron.

61. The method of claim 15, wherein the neuronal cell comprises a glycinergic neuron.

62. The method of claim 15, wherein the neuronal cell comprises a serotonergic neuron.

63. The method of claim 15, wherein the neuronal cell comprises a glutamatergic neuron.

64. The method of claim 15, wherein the neuronal cell comprises a peptidergic neuron.

65. A method of screening for substances that can inhibit neuronal cell death comprising:

- a) providing a recombinant *C. elegans* that expresses a detectable marker in a neuronal cell;
- b) exposing said *C. elegans* to a known neurotoxin and a candidate substance;
- c) detecting expression of the marker; and
- d) comparing the expression of the marker to the expression of the marker in the absence of the candidate substance.

66. The method of claim 65, wherein the *C. elegans* is exposed to the neurotoxin prior to the candidate substance.

67. The method of claim 65, wherein the *C. elegans* is exposed to the candidate substance prior to the neurotoxin.

68. The method of claim 65, wherein the detectable marker is a green fluorescent protein.

69. The method of claim 65, wherein the detectable marker is a yellow fluorescent protein.

70. The method of claim 65, wherein the detectable marker is a blue fluorescent protein.

71. The method of claim 65, wherein the detectable marker is a red fluorescent protein.

72. The method of claim 65, wherein the detectable marker is β -galactosidase.

73. The method of claim 65, wherein the detectable marker is under the control of a promoter.

74. The method of claim 65, wherein the detectable marker is an antigenic polypeptide.

75. The method of claim 65, wherein the detectable marker is under the control of a neuronal-specific promoter.

76. The method of claim 75, wherein the neuronal-specific promoter is a dopamine transporter promoter.

77. The method of claim 75, wherein the neuronal-specific promoter is a tyrosine hydroxylase promoter, a *cha-1* promoter, an *acr-2* promoter, an *unc-30* promoter, an *unc-4* promoter, or an *asi* promoter.

78. A method of screening candidate substances to identify a substance that can be used for prevention and/or therapy of neurodegenerative diseases comprising:

- a) obtaining a recombinant *C. elegans* that expresses a detectable marker in a neuronal cell under the control of a neuronal-specific promoter;
- b) exposing said *C. elegans* to a known neurotoxin and a candidate substance;
- c) detecting expression of the marker; and
- d) comparing the expression of the marker to the expression of the marker in the absence of the candidate substance.

79. The method of claim 78, wherein the *C. elegans* is exposed to the neurotoxin prior to the candidate substance.

80. The method of claim 78, wherein the *C. elegans* is exposed to the candidate substance prior to the neurotoxin .

81. The method of claim 78, wherein the neurodegenerative disease is selected from Parkinson's disease, Alzheimer's disease, Huntington's disease, a transmissible spongiform encephalopathy (TSE), a familial amyloid polyneuropathy (FAP), a prion diseases, a Tauopathy, a Trinucleotide disease, amyolateral sclerosis (ALS) or multiple system atrophy.

82. The method of claim 78, wherein the detectable marker is a green fluorescent protein.

83. The method of claim 78, wherein the detectable marker is a yellow fluorescent protein.

84. The method of claim 78, wherein the detectable marker is a blue fluorescent protein.

85. The method of claim 78, wherein the detectable marker is a red fluorescent protein.

86. The method of claim 78, wherein the detectable marker is β -galactosidase.

87. The method of claim 78, wherein the detectable marker is under the control of a promoter.

88. The method of claim 78, wherein the detectable marker is an antigenic polypeptide.

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89. The method of claim 78, wherein the detectable marker is under the control of a neuronal-specific promoter.

5 90. The method of claim 78, wherein the neuronal-specific promoter is a dopamine transporter promoter.

91. The method of claim 78, wherein the neuronal-specific promoter is a tyrosine hydroxylase promoter, a *cha-1* promoter, an *acr-2* promoter, an *unc-30* promoter, an *unc-4* promoter, or an *asi* promoter.
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92. A method of screening for substances that modulate dopamine transporter function comprising:

- 15 a) obtaining a recombinant *C. elegans* that expresses a detectable marker in a dopaminergic neuronal cell;
- b) exposing said *C. elegans* to a candidate substance;
- c) exposing said *C. elegans* to a neurotoxin that requires a dopamine transporter for intracellular access; and
- 20 d) detecting any change in the expression of the GFP after step c).

93. The method of claim 92, wherein the candidate substance blocks transport by the dopamine transporter.

94. The method of claim 92, wherein the candidate substance increases transport by the dopamine transporter.
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95. The method of claim 92, wherein the neurotoxin is an addictive substance.

96. The method of claim 92, wherein the addictive substance is selected from cocaine, amphetamines, methyl-phenidate.
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97. The method of claim 92, used to identify substances that provide therapy for neurological diseases involving dopamine transporter function.

5 98. The method of claim 97, wherein the neurological diseases involving dopamine transporter function are Schizophrenia, addiction disorders, attention deficit hyperactivity disorder, psychoses, Tourette's syndrome, or Parkinson's disease.

99. A method of screening for molecules that modulate neuronal signaling comprising:

- 10 a) obtaining a recombinant *C. elegans* that expresses a detectable protein in a neuronal cell which is a knockout and/or a mutant for a component of neuronal signaling;
- 15 b) obtaining a second recombinant *C. elegans* that expresses a detectable protein in a neuronal cell which is a or a second mutant for a component of neuronal signaling;
- c) comparing the differences in neuronal viability when exposed to a neurotoxic substance in the *C. elegans* of step a) with the *C. elegans* of step b); and
- 20 d) identifying the genetic component of the mutation.

100. The method of claim 99, further comprising isolating the genetic component.

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